REMARKS

Claims 1-25 constitute the pending claims in the present application. Claims 1-21 have been withdrawn by the Examiner for being directed to non-elected inventions pursuant to 37 CFR 1.142(b). Claims 22-25 are currently under examination.

Support for amended claim 22 may be found throughout the application as originally-filed, for example on page 6, lines 12-16; page 7, lines 12-26; and page 8, lines 1-2. Claim 24 has been amended solely to correct dependency of the claim and does not add any new matter.

Issues raised by the Examiner will be addressed below in the order they appear in the prior Office Action.

1. Applicants hereby request entry of the Copy of Papers Originally Filed dated June 21, 2002 (*See* attached). Applicants declare that the copy is a complete and accurate copy of the originally filed documents submitted.

IDS

2. Applicants thank the Examiner for noting the citation error for IDS reference A6. Applicants hereby submit the full citation for IDS reference A6 and request that the citation be place of record on the US-1449.

Leveugle, B. et al., *Proceedings of the American Association for Cancer Research Annual Meeting*, "PSA-directed Immunotherapy of Prostate Cancer", **39**: 355, March 1998.

35 USC § 112, second paragraph

3. Claims 22-25 were asserted as being rejected under 35 USC § 112, second paragraph, as being indefinite in the recitation of:

a. "diagnosing the efficacy" as recited in independent claim 22.

Applicants assert that the amendment to claim 22 obviates the rejection in view of the disclosure in the specification, for example, at pages 13-14, that the embodiments of claim 22 are drawn to a method of diagnosing the efficacy of the xenotypic antibody treatment. Efficacy as used in this aspect should be interpreted to encompass the definition at lines 4-5 of page 6, wherein efficacy is delayed progression or extension of life. Additionally, the method of claim 22 is clearly illustrated, for example, on page 14, wherein the favorable diagnosis of xenotypic antibody therapy is indicated by a 1.5 fold higher increase in T cell responses to the antigen. Applicants respectfully assert that this diagnosis is not a prediction of the time at which relapse occurs. Applicants respectfully request reconsideration and withdrawal of this rejection.

b. "favorable diagnosis" as recited in independent claim 22.

Applicants contend that the administration of a placebo is not a necessary step; however, one skilled in the art would know "the time after administration of a placebo when relapse occurs". There are well-established relapse times that may be found throughout the literature. Applicants respectfully request reconsideration and withdrawal of this rejection.

c. "T helper response" as recited in dependent claim 24 lacked antecedent basis in base claim 22.

Applicants have amended this claim to correct the dependency of the claim, thereby obviating the rejection. Applicants respectfully request reconsideration and withdrawal of this rejection.

35 USC § 103(a)

4. Claims 22-25 are asserted as being rejected under 35 U.S.C. § 103 (a) over Madiyalakan et al. (WO 97/42973) in view of Goletz et al. (U.S. Patent 5,997,869).

The Examiner states on page 7 of the Office Action that Madiyalakan et al. describe administration of a murine antibody specific for a tumor-associated antigen wherein a complex is created and produces an effective immune response that was not effective before administration of the antibody. The resulting immune response includes, among others, a T cell response (*see* paragraph 1).

The Examiner states on page 6, continuing to page 7 of the Office Action that due to the indefinite nature of the claims (see 112, second above), the claims are being interpreted to mean a method of determining if a T cell response was generated after xenotypic antibody administration and if there is an increased survival of the patients when administered to the patient.

Applicants direct the Examiner to the amendment to the claims and the arguments set forth *supra* with respect to 35 USC 112, second paragraph, to clarify the meaning of the terms of the claims which obviate Madiyalakan et al. as a prior art reference.

Applicants assert that Madiyalakan et al. do not teach or suggest testing of T cell responses for the purposes of measuring efficacy of the treatment to justify continued treatment. This is evidenced by the fact that it does not compare T cell responses before treatment to T cell responses after treatment as required by claim 22. The teachings of Madiyalakan et al. also differ from the instant claims in that they do not teach or suggest the testing of the T cell response before administration of the murine antibody or after administration as a diagnosis of efficacy to continue treatment. Such a teaching cannot be extrapolated to include within its scope the instant claims which recite a method for diagnosing the efficacy of a xenotypic antibody-mediated immunotherapy. Nor does Madiyalakan et al. provide any teachings to motivate one of ordinary skill in the art at the time the invention was made to even try such a diagnostic method.

The Examiner states on page 7 of the Office Action that Goletz et al. teach methods to immunize humans to induce cytotoxic T lymphocytes (see paragraph 2), and further, in paragraph 4 of page 7 and lines 1-11 of page 8 that Goletz et al. teach administration of a xenotypic antibody.

Applicants assert that Goletz et al. teach administration of a synthetic **peptide** specific for a genetic mutation where the peptide produces an immune response in the patient that is categorized as a cytotoxic T cell response. Further, Goletz et al. do not discuss any treatment with a xenotypic antibody, nor do they disclose measuring T cell responses after therapy and comparing them to the previous measurement to justify continued treatments. Teachings of synthetic peptides cannot be extrapolated as being the same as a xenotypic antibody. Thus, the

Goletz et al. references is non-analogous art and cannot make up the deficiencies of Madiyalakan et al.

The scope of claims 22- 25 encompasses the testing of an initial T cell response in a patient, who has a disease associated with an antigen to which the antibody binds prior to administering a xenotypic antibody, administering the xenotypic antibody, and then testing the patient's T cell response to the antigen. A higher T cell response than the initial measurement would indicate a favorable efficacy of treatment and justify administering further treatments with the xenotypic antibody.

One or ordinary in the art would not be motivated to combine the non-analogous references of Madiyalakan et al. and Goletz et al. to arrive at the claimed invenetion. The references involve two very distinct technologies, administration of a murine antibody for treatment of a disease associated with an antigen (Madiyalakan et al.) and administration of a synthetic **peptide** for treatment of disease associate with a mutated gene (Goletz et al.). The teachings of each reference either alone, or in combination do not teach every aspect of the claimed invention.

Consequently, in the absence of a motivation to combine the references, one of ordinary skill in the art would not have a reasonable expectation of success that combining the teachings of the references would have a reasonable expectation of success when contemplating the instant claims.

Applicants have amended the claims solely to further prosecution and reserve the right to pursue any canceled subject matter in a future application. In view of the amendment to the claims and the arguments set forth *supra*, Applicants respectfully request reconsideration and withdrawal of the rejection.

5. Claims 22-25 are asserted as being rejected under 35 U.S.C. § 103 (a) over Madiyalakan et al. (U.S. 6,241,985) in view of Goletz et al. (U.S. Patent 5,997,869).

The Examiner states on page 8 of the Office Action that Madiyalakan et al. teach the administration of a mouse antibody which led to increase in cytotoxic T lymphocytes in human cancer patients and stimulates both a humoral and cellular response and administration of the xenotypic antibody lead to an increase in the mean survival of the patients.

Applicants direct the Examiner to the amendment to the claims and the arguments set forth *supra* with respect to 35 USC 112, second paragraph, to clarify the meaning of the terms of the claims which obviate Madiyalakan et al. as a prior art reference.

Madiyalakan et al. was cited as not teaching measuring the T cell response prior to administration of the antibody. Applicants assert that prior to administration of the antibody, a T cell response had not be induced, and therefore, could not be measures. It is unclear what response the Examiner means to measure. Further, the claims are drawn to a method of diagnosing the efficacy of a xenotypic antibody-mediated immunotherapy, not to the induction of an immune response by administration of a xenotypic antibody. The preamble of instant claim 22 sets the instant invention outside the scope of the teachings of Madiyalakan et al., which cannot be made up through the teachings of Goletz et al. Nor does Madiyalakan et al. provide any teachings to motivate one of ordinary skill in the art at the time the invention was made to even try such a diagnostic method.

Applicant's position regarding Goletz et al. has been set forth *supra*.

One or ordinary in the art would not be motivated to combine the references of Madiyalakan et al. and Goletz et al. to arrive at the claimed invention. The references involve two very distinct technologies, administration of a murine antibody for treatment of a disease associated with an antigen (Madiyalakan et al.) and administration of a synthetic **peptide** for treatment of disease associate with a mutated gene (Goletz et al.). The teachings of each reference either alone, or in combination do not teach every aspect of the claimed invention.

Consequently, in the absence of a motivation to combine the non-analogous references, one of ordinary skill in the art would not have a reasonable expectation of success that combining the teachings of the references would have a reasonable expectation of success when contemplating the instant claims.

Applicants have amended the claims solely to further prosecution and reserve the right to pursue any canceled subject matter in a future application. Applicants respectfully request reconsideration and withdrawal of the rejection.

CONCLUSION

In view of the foregoing amendments and remarks, Applicants submit that the pending claims are in condition for allowance. Early and favorable reconsideration is respectfully solicited. The Examiner may address any questions raised by this submission to the undersigned at 617-951-7000. Should an extension of time be required, Applicants hereby petition for same and request that the extension fee and any other fee required for timely consideration of this submission be charged to **Deposit Account No. 18-1945.**

Respectfully Submitted,

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